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J Tradit Chin Med 2014 August 15; 34(4): 445-449
ISSN 0255-2922
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CLINICAL STUDY

Effect of Yiqibushenhuoxue decoction on chronic obstructive pulmonary disease measured by St. George's respiratory disease questionnaire scores and forced expiratory volume

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Accepted: January 19, 2013

Abstract

OBJECTIVE: To investigate the effects of Yiqibushenhuoxue decoction on stable chronic obstructive pulmonary disease (COPD) by observing its influences on patients' quality of life and airway inflammation.

METHODS: Seventy patients with stable COPD were randomly divided into a treatment group (*n*= 35) treated with Yiqibushenhuoxue decoction plus Seretide and a control group (*n*=35) treated with Seretide only. The dosage of Yiqibushenhuoxue decoction was 100 mL each time, twice a day, and the dosage of Seretide was salmeterol 50 μg/fluticasone 250 μg twice a day. Both groups were treated for 12 weeks. Before and after the treatment, St George's respiratory disease questionnaire (SGRQ) scores, forced expiratory volume, and forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) were measured.

RESULTS: The SGRQ scores in both groups were significantly lower than those before treatment ($P<0.05$). After treatment, the total SGRQ scores and each subscore in the treatment group were significantly lower than those in the control group ($P<0.05$). The percentage of the predicted FEV_1% and FEV_1/FVC were higher in both groups, but no statistical differences were detected from before to after the treatment or between the two groups ($P>0.05$).

CONCLUSION: Yiqibushenhuoxue decoction could significantly decrease the SGRQ scores in patients with stable COPD, which suggests that it is able to improve patient symptoms.

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Key words: Pulmonary disease, chronic obstructive; Yiqibushenhuoxue decoction; Quality of life; Airway inflammation

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as "a preventable and treatable disease, which is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases".[1] The airway inflammation is related to a variety of physiological and pathological processes such as tissue damage, airway remodeling, high mucus secretion, and a lack of elasticity, and plays an important role in the pathogenesis of COPD.[2] At present, the treatment (including Western Medicine and integrative medicine therapy) of acute

exacerbations of COPD are somewhat effective. However, effective follow-up treatment during stable COPD, and to prevent relapses are urgently needed. Stable COPD treatment aims to alleviate symptoms, reduce the frequency and severity of attacks, improve pulmonary function, and improve the patients' quality of life.[3] While modern medicine is effective for stable COPD, some limitations still exist, such as side effects and limited long-term use. These side effects leave COPD patients with a lack treatment options and effective herbs, which can lead to recurrent attacks and further development of the disease. In this randomized controlled clinical trial, we observed the influences of Yiqibushenhuoxue decoction on the quality of life, pulmonary function, and airway inflammation of COPD patients, and compared them with those of conventional treatment.

MATERIALS AND METHODS

Demographics

Seventy outpatients of the Department of Respiratory Medicine in the First Affiliated Hospital of Heilongjiang University of Chinese Medicine from February 2012 to June 2013, were divided into a treatment and control group by means of random number table, with 35 patients in each. This study was approved by the ethics committee of the First Affiliated Hospital of Heilongjiang University of Chinese Medicine. All patients signed an informed consent form.

Diagnostic criteria

The diagnostic criteria for COPD was based on the global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease updated in 2011.[1] Clinical severity classification standard was set according to the guidelines of diagnosis and treatment of chronic obstructive pulmonary disease.[3] The specific grading criteria are as follows: mild cases: forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC)<70%, FEV_1% ≥80%, with or without chronic cough, sputum symptoms; moderate cases: FEV_1/FVC<70%, 50%≤FEV_1%<80%, with or without chronic cough, sputum, dyspnea symptoms.

The diagnostic criteria for lung and kidney *Qi* deficiency and blood stasis in terms of Traditional Chinese Medicine (TCM) were based on the guidelines[4] for the TCM diagnosis and treatment of chronic obstructive pulmonary disease. Patients with more than two of 1-3, more than two of 4-7, and more than one of 8-11 were considered to have lung and kidney *Qi* deficiency and blood stasis. 1: wheezing or shortness of breath, which is aggravated after activity; 2: lack of power or sweating, which is aggravated when moving; 3: susceptible to colds, and a serious attack by wind; 4: soreness and weakness of the waist and knees; 5: tinnitus, dizziness, or edema of the face; 6: frequent urination, nocturia, or cough urination; 7: pale tongue and white coated tongue, deep and thready pulse, or weak pulse; 8: dark purple complexion; 9: cyanosis of the lips and nails; 10: dark purple tongue, or tongue with petechia; 11: circuitous or coarse sublingual vein.

Inclusive criteria

This study recruited patients with COPD and lung and kidney *Qi* deficiency and blood stasis. All patients were classified as having mild or moderate disease that was stable for more than half a month.

Exclusive criteria

Patients were excluded if they met any of the following criteria: were definitely diagnosed of bronchial asthma; had serious heart, liver, or kidney functional impairment; were pregnant or currently lactating; or had an allergic constitution or were allergic to any herbs used in this study.

Rejected criteria

Patients were removed from the study if they met any of the following criteria: they failed to use the prescribed medication so that we were unable to judge the curative effect; their data were not complete, which could affect efficacy or safety judgments; or they did not meet the inclusive criteria after inclusion.

Suspended and removal criteria

Patients were suspended and removed if they: could not cooperate throughout the study; had serious adverse reactions or serious complications; or had disease exacerbations and needed to take active treatment measures.

Therapy

Both of the treatment and the control group were given Salmeterol Xinafoate and fluticasone propionate powder for inhalation (Glaxo Smith Kline Plc, UK), salmeterol 50 μg/fluticasone 250 μg, twice a day. In addition to the basic medication, patients in the treatment group were also given an herbal decoction, which was composed of: Dangshen (*Radix Codonopsis*) 20 g, Huangqi (*Radix Astragali Mongolici*) 20 g, Wuweizi (*Fructus Schisandrae Chinensis*) 15 g, Shudihuang (*Radix Rehmanniae Praeparata*) 15 g, Buguzhi (*Fructus Psoraleae*) 15 g, Yinyanghuo (*Herba Epimedii Brevicornus*) 15 g, Ziwan (*Radix Asteris Tatarici*) 15 g, Kuandonghua (*Flos Farfarae*) 15 g, Zisuzi (*Fructus Perillae Argutae*) 15 g, Banxia (*Rhizoma Pinelliae*) 10 g, Sumu (*Lignum Sappan*) 10 g, Shanzhuyu (*Fructus Corni*) 15 g, Huangjing (*Rhizoma Polygonati Sibirici*) 15 g, and Gancao (*Radix Glycyrrhizae*) 5 g. The above herbs were decocted and concentrated to 200 mL juice. The dosage of herbal decoction was 200 mL every day with 100 mL taken orally in the morning and evening. The herbal decoction was prepared by the Pharmaceutical Factory of the First Affiliated Hospital of Heilongjiang University of Chinese Medicine. Both groups were treated for 12 weeks.

Measurement

The measurement included St George's respiratory disease questionnaire (SGRQ).[5] This questionnaire was divided into three parts: respiratory symptoms, activity ability, and impacts of the disease. There were 50 items in total to evaluate the patients' quality of life. The higher the score is, the worse the health status of the patient. Pulmonary function tests, FEV_1/FVC and FEV_1% were tested and recorded on the first visit and again after the 12 week treatment.

Data analysis

Data were analyzed with SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). The data were represented as ($\bar{x} \pm s$). *t*-test was used to compare data between groups. $P<0.05$ was considered significant.

RESULTS

Comparison of the general statistics before treatment

Seventy patients recuited in this study were randomly divided into a treatment and control group with 35 patients in each. All the subjects recuited were at the age of 48-74 years old. The illness course of the treatment group was 2-10 years, while that of the control group was 2-12 years. After the trial, all the patients who completed the trial in two groups (treatment group 32 cases, control group 33 cases) conducted a follow-up, and showed good clinical effect with no adwerse reactions. The flow diagram of the trial is shown in Figure 1.

There were no significant differences in gender, age, course of disease, or severity level between two groups before treatment ($P>0.05$) as shown in Table 1.

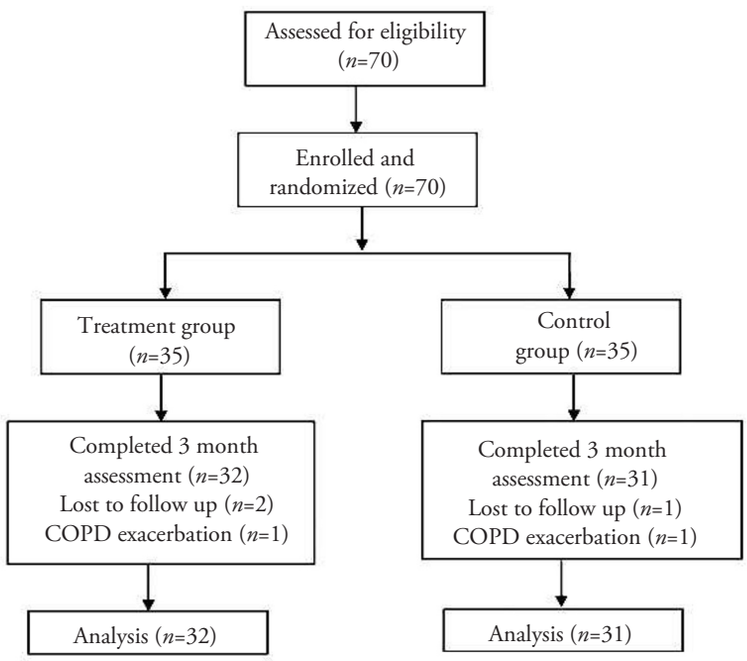

Figure 1 Flow diagram of the trial
COPD: chronic obstructive pulmonary disease.

Comparison of SGRQ scores before and after treatment

There were no statistical significances in the total SGRQ score and its three parts between two groups before treatment ($P>0.05$). The SGRQ scores after treatment in both groups were significantly lower than those before treatment ($P<0.05$). There was a statistical difference between the two groups in the total scores, the respiratory symptom score, activity ability score, and impacts of the disease score after treatment ($P<0.05$) (Table 2).

Comparison of FEV_1% and FEV_1/FVC before and after treatment

There were no statistical differences in FEV_1% and FEV_1/FVC between two groups before treatment ($P>0.05$). The FEV_1% and FEV_1/FVC after treatment were both higher in the two groups compared with before treatment. However, this increase was not statistically significant ($P>0.05$). There were no statistical differences between two groups in FEV_1% and FEV_1/FVC after treatment ($P>0.05$) (Table 3).

DISCUSSION

COPD is a common respiratory disease. Many patients' clinical symptoms are not well controlled as the disease has recurrent attacks, and the pulmonary function and quality of life of patients tend to decline. Many patients eventually succumb to diseases related to the lung. Treatment during the stable period aims at reducing symptoms and future risks, and can effectively reduce the frequency of acute attacks. The etiology and pathogenesis of COPD are very complex. Li *et al*[6] summarized the pathogenesis of COPD as "weakened

Table 1 Comparison of the general situation before treatment

Group	*n*	Gender		Age (years)	Course of disease (years)	Severity level	
		Male	Female			Mild	Moderate
Treatment	32	17	15	63.0±6.1	5.6±2.8	12	20
Control	33	17	16	64.8±6.4	5.1±2.6	10	23
P value	-	0.897		0.230	0.482	0.540	

Notes: the treatment group was treated with Yiqibushenhuoxue decoction (100 mL each time, twice a day) and Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day); the control group was treated with Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day).

Table 2 Comparison of SGRQ scores ($\bar{x}\pm s$)

Group	*n*	Time	Respiratory symptom	Activity ability	The impacts of disease	Total score
Treatment	32	Before treatment	45±12[a]	31±6[a]	21±6[a]	28±9[a]
		After treatment	30±10[bc]	19±4[bc]	13±6[bc]	20±8[bc]
Control	33	Before treatment	45±11	30±6	23±6	29±9
		After treatment	37±8[c]	22±5[c]	16±6[c]	25±9[c]

Notes: the treatment group was treated with Yiqibushenhuoxue decoction (100 mL each time, twice a day) and Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day); the control group was treated with Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day). SGRQ: George's respiratory disease questionnaire. [a]*P*>0.05, compared with the control group before treatment; [b]*P*<0.05, compared with the control group after treatment; [c]*P*>0.05, compared with itself before treatment.

Table 3 Comparison of FEV_1% and FEV_1/FVC ($\bar{x}\pm s$)

Group	*n*	Time	FEV_1%	FEV_1/FVC
Treatment	32	Before treatment	69±12[a]	61±4[a]
		After treatment	70±12[bc]	63±4[bc]
Control	33	Before treatment	68±12	61±4
		After treatment	70±12[c]	63±4[c]

Notes: the treatment group was treated with Yiqibushenhuoxue decoction (100 mL each time, twice a day) and Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day); the control group was treated with Seretide (one inhale salmeterol 50 μg/fluticasone 250 μg each time, twice a day). FEV_1%: the percentage of the predicted forced expiratory volume in 1 second; FEV_1/FVC: forced expiratory volume in 1 second/forced vital capacity. [a]*P*>0.05, compared with the control group before treatment; [b]*P*>0.05, compared with the control group after treatment; [c]*P*>0.05, compared with before treatment.

body resistance and accumulated pathogens." Weakened body resistance refers to the deficiency of lung, spleen, and kidney. In this weakened body resistance, pulmonary deficiency is the beginning, kidney deficiency is the base, and *Qi* deficiency is the origin, while accumulated pathogens include phlegm and blood stasis. Chronic illness caused by accumulated pathogens is very difficult to treat and damages healthy *Qi*, to the extent that healthy *Qi* becomes more deficient and pathogens further accumulate. At the beginning of the disease, the dispersing and descending function of the lung is impaired because of exogenous pathogens. Then, lung injury caused by chronic cough leads to pulmonary *Qi* deficiency. As the disease progresses, phlegm is produced and injures the lung because the spleen is so deficient that it cannot transport and transform water and fluid. Furthermore, chronic illness damages the kidney so that kidney fails to receive *Qi*. This dysfunction of the kidney leads to additional cough and difficulty breathing. Healthy *Qi* becomes deficient because of chronic illness so its promoting and warming function declines. Humor clusters into phlegm and blood stops running, which turns into stasis. Li *et al*[7] found, by studying the distribution of patterns in 209 COPD patients, that the phlegm was the most common excess pattern, and blood-stasis was second.

The treatment of COPD with TCM has significant clinical effects, especially in patients with stable COPD. Relevant clinical and basic studies having received increasing attention, and having made some progress.[8] According to the pathological features of stable COPD, we established the treatment principle of "benefiting the lung and kidney, invigorating the circulation and resolving phlegm." In this decoction, the monarch herbs, Dangshen (*Radix Codonopsis*) replenishes *Qi* and Huangqi (*Radix Astragali Mongolici*) tonifies the lung, while securing the exterior, enhancing the efficacy of the total complement of lung *Qi*. Wuweizi (*Fructus Schisandrae Chinensis*) can converge the lung and relieve cough, preventing lung *Qi* from further consumption, and can also nourish kidney yin.

Shudi can tonify the kidney to receive *Qi* and relieve breathing. Buguzhi (*Fructus Psoraleae*) warms the kidney to receive *Qi*. Huangjing (*Rhizoma Polygonati Sibirici*) nourishes *Yin* and moistens the lung, nourishes the kidney, strengthens the essence, and increases in efficacy with Jin and Shui. Kuandonghua (*Flos Farfarae*) and Ziyuan can moisten the lung, relieve cough and reduce phlegm. Zisuzi (*Fructus Perillae Argutae*) can descend the adverse-rising *Qi*, resolve phlegm, and relieve cough and breathing. Banxia (*Rhizoma Pinelliae*) can remove dampness to reduce phlegm. Each of these herbs are ministerial herbs. The adjuvant herbs are Sumu (*Lignum Sappan*), which is used for promoting blood circulation and removing blood stasis, and Shanzhuyu, for nourishing kidney *Yin*. Gancao (*Radix Glycyrrhizae*), the conductant drug, can reconcile the various herbs, relieve cough, resolve phlegm. Various herbs used in the decoction can benefit the lung and kidney, invigorating the circulation, and resolving phlegm. Modern pharmacology studies have shown that Dangshen has various physiological functions, including anti-inflammation, immune regulation, and anti-hypoxic.[9,10] Moreover, astragaloside Ⅳ, the principal active component of Huangqi (*Radix Astragali Mongolici*), can effectively restrain the chronic asthma induced by ovalbumin, decrease airway sensitivity, alleviate airway fibrosis, remove thickened smooth muscle, and inhibit goblet cell hyperplasia. The combined use of Dangshen (*Radix Codonopsis*) and Huangqi (*Radix Astragali Mongolici*) can amplify their range of application and increase efficacy.[11] Yinyanghuo (*Herba Epimedii Brevicornus*) can correct axis disorders, promote the anti-inflammatory and immune capacity of the body, and resist the fibrosis and remodeling of the airway.[12] Sumu (*Lignum Sappan*) can optimize the immune response at the cellular and molecular level, and has anti-inflammatory, microcirculatory, and antioxidative properties.[13]

We showed that Yiqibushenhuoxue decoction could significantly lower the GRDQ scores of patients with stable COPD. However, there were no statistical differences between the two groups in FEV_1% and FEV_1/FVC before and after treatment. This implies that Yiqibushenhuoxue decoction could significantly improve a patients' symptoms as measured by the SGRQ scores only. Although the FEV_1% and FEV_1/FVC improved, this change was not statistically significant compared with before treatment, possibly because of the study was too short. Whether Yiqibushenhuoxue decoction can change the trend of lung function decline in patients with COPD should be studied further. Because of a relatively small study sample size and short observational time, studies with large samples and longer durations should be conducted to further substantiate our findings.

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